

REMARKS

Claims 1- 24 have been cancelled without prejudice or disclaimer to the subject matter contained therein. Applicants retain the right to assert any cancelled or amended subject matter in this or a continuation or divisional application.

Support for the new claims can be found throughout the application as-filed. Specifically, and by way of nonlimiting example, claims 1, 2, 6, 9 and 14, as well as paragraphs [0008] and [0024], both of the application as-filed.

As such, the amendments do not introduce any new matter within the meaning of 35 USC §132. Therefore, entry of the amendments is respectfully requested.

Information Disclosure Statement

The Examiner has stated the information disclosure statement filed on March 9, 2005 did not provide copies of the three non-patent literature references cited therein. Applicants respectfully submit that a review of the U.S. Patent Office electronic file wrapper maintained on Private PAIR does identify three non-patent literature references to Larsen et al., Lunday et al. and Rabilloud et al. Each reference appears to be in a legible and complete format.

Therefore, Applicants submit that the information disclosure statement filed on March 9, 2005 is in compliance with 37 CFR 1.98(a)(2) and consideration of all of the references contained therein by the Examiner is respectfully requested.

Sequence Compliance

The Examiner has stated that the application contains sequence disclosures that are encompassed by the definitions from nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), but that the application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Applicants respectfully submit that this is the second Notice to Comply with Requirements regarding sequence listing received in this application. The first notice can be found in the U.S. Patent Office electronic file wrapper on the date of June 14, 2005. A response to the notice was filed on July 12, 2005, and this document is also available in the electronic file wrapper on that date. This response has not been acknowledged by the Office or by this Examiner. Applicants respectfully request acknowledgement of same.

Drawings

Applicants respectfully submit that the specification has been amended to add reference to Figures 2, 4A, 4B and 4C.

Claim Objections

The Examiner has objected to claims 1, 6, 8, 10 and 16 based on various formalities.

All claims in the application have been cancelled, and Applicants submit that each of the items identified in the objections has been deleted or corrected in the new claims.

As such, the Examiner is respectfully requested to withdraw these objections.

Claim Rejections under 35 USC §112, second paragraph

The Examiner has rejected to claims 1-3, 6-12, 14-12 and 17- 21 as being indefinite for failing to particularly point out and distinctly claim the claimed subject matter.

Applicants traverse this rejection.

All claims in the application have been cancelled, and Applicants submit that basis for each of the rejections has been deleted or corrected in the new claims.

As such, the Examiner is respectfully requested to withdraw these rejections.

Claim Rejection under 35 USC §103(a)

The Examiner has rejected claims 1-3, 6-12 and 14-21 as being unpatentable over Merrill (US Patent No. 4,405,720), in view of Tsuzuki et al. (US Patent No. 5,922,529), Diwu et al. (US Patent No. 6,329,205), and Rabilloud (1990, "Mechanisms of Protein Silver Staining in Polyacrylamide Gels..." Electrophoresis, 11:785-794.

Applicants traverse this rejection.

All claims in the application have been cancelled, and Applicants submit that basis for the rejection has been deleted or corrected in the new claims.

As such, the Examiner is respectfully requested to withdraw this rejection.

Assuming the Examiner disagrees with the forgoing, Applicants hereby submit the following for the Examiner's consideration.

The instant subject matter, as presently claimed, is directed to a method for silver staining for detecting proteins, comprising the steps of applying the proteins to be detected onto or into a support for detection; incubating the proteins on or in the support with **a bifunctional agent having the general formula X-R wherein R is a hydrophobic moiety and X is a reducing moiety**; washing the support; incubating the support with the proteins thereon or therein with a solution containing silver ions; and applying a developing solution, characterized in that the hydrophobic moiety of the bifunctional agent is an acyloxy-radical of the general formula $-O-CO-C_nH_{(2n+1)}$ wherein n is 8 -21 and the reducing moiety of the bifunctional agent is ascorbic acid.

Applicants submit that in contrast to classical silver staining methods, the method according to the instant claims makes use of the bifunctional agent as defined above. Applicants submit that the claimed bifunctional agent can be used as a sensitizer in silver staining methods, i.e. a substitute for classical reagents, such as glutaraldehyde, DDT, dithionite and thiosulfate. See instant application as filed at paragraph [0008]. In contrast to these reagents, the instant bifunctional agent **does not bind covalently to the proteins to be detected**. This consequently **allows for subsequent mass spectrometrically detection of the proteins**. This claimed feature has not been identified in the cited art.

The bifunctional agent is defined as an agent with a hydrophobic moiety of the general formula $-O-CO-C_nH_{(2n+1)}$ wherein n is 8-21. With the claimed hydrophobic

moiety, the bifunctional agent can bind noncovalently to proteins. The bifunctional agent also contains ascorbic acid as the reducing agent. Such a reducing moiety is able to reduce silver ions used in silver staining methods. Examples of the claimed bifunctional agent are ascorbyl palmitate, ascorbyl stearate, ascorbyl myristate and ascorbyl laurate.

The Examiner states that none of the cited references dealing with silver staining methods discloses the use of agents such as ascorbyl palmitate or ascorbyl stearate. The Examiner has only pointed out Tsuzuki et al. teaching a **photothermographic material**. It is completely unclear why one of skill in the art would jump to and then rely on the teaching of Tsuzuki et al., since the teaching is contained in a huge laundry list which is populated with unusable examples.

As such, the skilled artisan, using the teachings of the cited references, would not arrive at the claimed subject matter, namely, a method of using the claimed bifunctional agent in a silver staining method.

Accordingly, the claimed methods are unobvious over the cited references and the Examiner is respectfully requested to reconsider and withdraw this rejection.

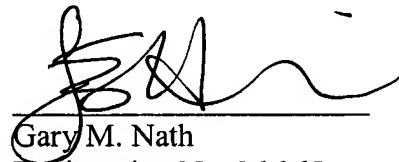
CONCLUSION

In view of the foregoing, Applicants respectfully submit that a full and complete response has been made.

The Examiner is welcomed to contact the undersigned attorney at the below-listed number and address with any questions or comments regarding this matter.

Respectfully submitted,

THE NATH LAW GROUP

A handwritten signature in black ink, appearing to read 'Gary M. Nath', is written over a horizontal line.

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